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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/502,984	02/11/00	LEO	P A-68126-1/RF

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FLEHR HOHBACH TEST
ALBRIGHT & HERBERT LLP
FOUR EMBARCADERO CENTER SUITE 3400
SAN FRANCISCO CA 94111-4187

EXAMINER

ZARA, J

ART UNIT	PAPER NUMBER
1635	10

DATE MAILED: 10/17/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)
	09/502,984	LUO ET AL.
	Examiner	Art Unit
	Jane Zara	1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 09 August 2001.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-19 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-19 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are objected to by the Examiner.

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

- Certified copies of the priority documents have been received.
- Certified copies of the priority documents have been received in Application No. _____.
- Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) Notice of References Cited (PTO-892)

16) Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____

18) Interview Summary (PTO-413) Paper No(s) _____

19) Notice of Informal Patent Application (PTO-152)

20) Other: _____

File

DETAILED ACTION

This Office action is in response to the communication filed August 9, 2001, Paper No. 9.

Claims 1-19 are pending in the instant application.

Response to Amendments and Arguments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4, 6-9 and 11-19 are rejected under 35 U.S.C. 102(e) as being anticipated by Stahl et al for the reasons of record set forth in the Office action mailed January 31, 2001, Paper No. 7.

Applicant's arguments filed August 9, 2001 have been fully considered but they are not persuasive. Applicants argue that, since the instant invention utilizes a computational modeling system that allows the generation of extremely stable proteins without necessarily disturbing the biological function of the protein itself, it (the instant invention) is distinct from the previously cited art (including Stahl et al) and furthermore would not be obvious to one of ordinary skill in the art. Contrary to Applicants' assertions, the instant invention is drawn to methods of functionally testing polypeptides for ligand binding, which polypeptides encode cell surface

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receptors which contain amino acid variations within them compared to previously characterized receptors with known ligand binding properties, as well as using mutagenesis approaches for receptors in ligand screening assays for the identification of new ligands. The combination of the techniques comprising polypeptide mutagenesis and the determination of an alteration of protein function, including ligand binding by receptors, has been used historically in protein biochemistry and structural biology (See Stahl especially at col. 9, line 31-col. 12, line 9). The aid of computer modeling in predicting alterations in protein function has been used traditionally in the art and has included a myriad of approaches which are still used, including techniques as rudimentary as sequence alignment, alanine scanning, or random mutagenesis, and more learned approaches including domain mapping, secondary structure predictions and a correlation with protein function, as well as higher order protein structure modeling (protein design automation) and allosterism. In addition, high throughput ligand binding assays are employed routinely in the art for both identifying binding or recognition motifs in proteins and in identifying new ligands. The combination of these techniques, computer modeling to guide protein mutagenesis followed by the empirical determination of alterations in protein function (including high throughput screening assays for ligand binding) would have been a matter of routine matter in the art at the time the invention was made.

Claims 1-4, 6-12 and 17-19 are rejected under 35 U.S.C. 102(e) as being anticipated by Jin et al for the reasons of record set forth in the Office action mailed January 31, 2001, Paper No. 7.

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Applicant's arguments filed August 9, 2001 have been fully considered but they are not persuasive. Applicants argue that, since the instant invention utilizes a computational modeling system that allows the generation of extremely stable proteins without necessarily disturbing the biological function of the protein itself, it (the instant invention) is distinct from the previously cited art (including Jin et al) and furthermore would not be obvious to one of ordinary skill in the art. Contrary to Applicants' assertions, the instant invention is drawn to methods of functionally testing polypeptides for ligand binding, which polypeptides encode cell surface receptors which contain amino acid variations within them compared to previously characterized receptors with known ligand binding properties, as well as using mutagenesis approaches for receptors in ligand screening assays for the identification of new ligands. The combination of the techniques comprising polypeptide mutagenesis and the determination of an alteration of protein function, including ligand binding by receptors, has been used historically in protein biochemistry and structural biology (See Jin especially at col. 10, lines 10-29). The aid of computer modeling in predicting alterations in protein function has been used traditionally in the art and has included a myriad of approaches which are still used, including techniques as rudimentary as sequence alignment, alanine scanning, or random mutagenesis, and more learned approaches including domain mapping, secondary structure predictions and a correlation with protein function, as well as higher order protein structure modeling (protein design automation) and allosterism. In addition, high throughput ligand binding assays are employed routinely in the art for both identifying binding or recognition motifs in proteins and in identifying new ligands.

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The combination of these techniques, computer modeling to guide protein mutagenesis followed by the empirical determination of alterations in protein function (including high throughput screening assays for ligand binding) would have been a matter of routine matter in the art at the time the invention was made.

Claims 1-4, 6-12, 18 and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by Ichijo et al for the reasons of record set forth in the Office action mailed January 31, 2001, Paper No. 7.

Applicant's arguments filed August 9, 2001 have been fully considered but they are not persuasive. Applicants argue that, since the instant invention utilizes a computational modeling system that allows the generation of extremely stable proteins without necessarily disturbing the biological function of the protein itself, it (the instant invention) is distinct from the previously cited art (including Ichijo) and furthermore would not be obvious to one of ordinary skill in the art. Contrary to Applicants' assertions, the instant invention is drawn to methods of functionally testing polypeptides for ligand binding, which polypeptides encode cell surface receptors which contain amino acid variations within them compared to previously characterized receptors with known ligand binding properties, as well as using mutagenesis approaches for receptors in ligand screening assays for the identification of new ligands. The combination of the techniques comprising polypeptide mutagenesis and the determination of an alteration of protein function, including ligand binding by receptors, has been used historically in protein biochemistry and structural biology (See Ichijo especially at col. 5, line 14-col. 6, line 60; col. 8, lines 15-23). The

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aid of computer modeling in predicting alterations in protein function has been used traditionally in the art and has included a myriad of approaches which are still used, including techniques as rudimentary as sequence alignment, alanine scanning, or random mutagenesis, and more learned approaches including domain mapping, secondary structure predictions and a correlation with protein function, as well as higher order protein structure modeling (protein design automation) and allosterism. In addition, high throughput ligand binding assays are employed routinely in the art for both identifying binding or recognition motifs in proteins and in identifying new ligands. The combination of these techniques, computer modeling to guide protein mutagenesis followed by the empirical determination of alterations in protein function (including high throughput screening assays for ligand binding) would have been a matter of routine matter in the art at the time the invention was made.

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stahl et al, Jin et al and Ichijo et al as applied to claims 1-4 and 6-19 above, and further in view of Ochoa et al for the reasons of record set forth in the Office action mailed January 31, 2001, Paper No. 7.

Applicant's arguments filed August 9, 2001 have been fully considered but they are not persuasive. Applicants argue that, since the instant invention utilizes a computational modeling system that allows the generation of extremely stable proteins without necessarily disturbing the biological function of the protein itself, it (the instant invention) is distinct from the previously cited art (including Stahl, Jin and Ichijo as cited above) and furthermore would not be obvious to one of ordinary skill in the art. Contrary to Applicants' assertions, the instant invention is drawn

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to methods of functionally testing polypeptides for ligand binding, which polypeptides encode cell surface receptors which contain amino acid variations within them compared to previously characterized receptors with known ligand binding properties, as well as using mutagenesis approaches for receptors in ligand screening assays for the identification of new ligands. The combination of the techniques comprising polypeptide mutagenesis and the determination of an alteration of protein function, including ligand binding by receptors, has been used historically in protein biochemistry and structural biology. The aid of computer modeling in predicting alterations in protein function has been used traditionally in the art and has included a myriad of approaches which are still used, including techniques as rudimentary as sequence alignment, alanine scanning, or random mutagenesis, and more learned approaches including domain mapping, secondary structure predictions and a correlation with protein function, as well as higher order protein structure modeling (protein design automation) and allosterism. In addition, high throughput ligand binding assays are employed routinely in the art for both identifying binding or recognition motifs in proteins and in identifying new ligands, and such assays routinely employed in the art include in vitro binding assays in solution as well as solid phase assays involving either receptors tethered to the surface of cells via attachment to some of (membrane inserted) anchor domain, or alternatively via covalent attachment to a solid surface (e.g. see Ochoa at col. 4, lines 25-44). The combination of these techniques, computer modeling to guide protein mutagenesis followed by the empirical determination of alterations in protein

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function (including high throughput screening assays for ligand binding) would have been a matter of routine matter in the art at the time the invention was made.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be

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retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820**. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on **(703) 308-0447**. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is **(703) 305-3413**. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is **(703) 308-0196**.

JZ



ANDREW WANG
PRIMARY EXAMINER

October 16, 2001